

USPQ 668 (CCPA 1969); *Lindemann Maschinefabrik GMBH v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984). It is further noted that satisfaction of the enablement requirement is not precluded by the necessity of some experimentation, such as routine experimentation. The key word here is "undue" not "experimentation". *In re Angstadt*, 190 USPQ 214 (CCPA 1976). Indeed, a considerable amount of experimentation is permissible if it is merely routine, or if the specification provides a reasonable amount of guidance to the direction in which the experimentation should proceed. *In re Jackson*, 217 USPQ 804 (Bd. App. 1982).

Applicant's independent claim 1, as amended, is directed to a genetically engineered plant, comprising a recombinant nucleic acid that encodes an enzyme in a plant Vitamin C biosynthesis pathway, wherein said enzyme is selected from a group of four enzymes. As such, claim 1 (and dependent claims 2-8) is not drawn to a method, and does not recite the limitation of overexpression. Further, claim 1, as amended, is expressly limited to a group of only four enzymes. Similarly, Applicant's independent claim 9 is directed to a genetically engineered plant, comprising a recombinant nucleic acid that encodes GDP-mannose pyrophosphorylase. As such, claim 9 (and dependent claims 10-15) does not recite the limitation of overexpression. Further, claim 9 is expressly limited to a single enzyme. Independent claim 16, as amended, is directed to a method of increasing the level of Vitamin C in a plant comprising the step of engineering said plant to express an enzyme in a plant Vitamin C biosynthesis pathway, wherein said enzyme is selected from a group of four enzymes. As such, claim 16 (and dependent claims 17-22) is directed to a method, but it does not recite the limitation of overexpression. Further, claim 16, as amended, is expressly limited to a group of only four enzymes.

The Examiner asserts that the instant specification, while discussing expression of an *Arabidopsis* gene encoding GMPase in vtcl mutants of *Arabidopsis*, fails to provide guidance for successful overexpression of that gene in wild-type plants, and that overexpression of a gene in plants is unpredictable. The Examiner thus concludes that, as Applicant's gene encoding GMPase was not expressed in wild-type plants, the unpredictability associated with overexpression of genes in plants has not been overcome.

The Examiner's attention is drawn to the fact that Applicant's claims, as amended, do not encompass expression or overexpression of any gene in "wild-type plants". Rather, the claims

are directed to genetically engineered plants, not wild-type plants. Therefore, no enablement regarding expression or overexpression of a gene in wild-type plants is required. Further, "overexpression" is not a feature of any of the claims, as amended. Moreover, it is respectfully submitted that the Examiner's assertion that the unpredictability associated with overexpression of genes in plants has not been overcome is mistaken, in that Applicant's gene encoding GMPase was transformed into plants, thereby generating genetically engineered plants having increased levels of Vitamin C, relative to the progenitor plants. See Applicant's specification at page 13, line 24, through page 17, line 3. Thus, clearly, Applicant's GMPase can be expressed in plants, and clearly such plants have increased levels of Vitamin C, thus overcoming any alleged unpredictability. Although in the past, in some cases expression of foreign genes in plants has been unpredictable, the current state of the art is such that, using routine methods that are well known in the art, one of ordinary skill in the art can predictably transfer into and express virtually any gene (including bacterial genes and other genes of non-plant origin) in plants (including both monocots and dicots). Indeed, the Examiner appears to have admitted such in applying the rejections under sections 102 and 103.

The Examiner asserts further that: 1) the only gene encoding GMPase taught in the instant specification is from *Arabidopsis*, 2) the instant specification fails to teach any other gene encoding any other enzyme involved in vitamin C biosynthesis, 3) it also fails to teach or suggest any method of overexpressing any enzyme other than by transformation of a gene into a plant, and 4) fails to provide guidance for the sequence of the gene encoding GMPase. Thus, the Examiner concludes that the invention appears to employ novel plasmid encoding GMPase contained in microorganisms, and that a deposit is required for enablement purposes.

It is respectfully submitted that genes encoding GMPase (including that of *Arabidopsis* and other species), as well as the other enzymes in the Vitamin C pathway, are well known in the art and, as such, are not required to be disclosed in Applicant's specification. However, Applicant's Figure 1 and the specification at page 4, lines 12-16, disclose the enzymes in the Vitamin C pathway. Further, Applicant's specification provides ample guidance for the sequence of the gene encoding GMPase at page 11, lines 5-8, wherein the GenBank accession number is provided. Thus, one of ordinary skill in the art would know the sequence of the GDP-mannose pyrophosphorylase, as it is well known in the art, and ample guidance thereto also is disclosed in

Applicant's specification. Finally, the claims, as amended, do not encompass any method for expressing a recombinant gene in a plant, other than that of transformation of a gene into a plant. Therefore, no guidance regarding any other methods is required.

In view of the above, the Examiner is requested to note that the specification contains sufficient matter to support the genetically engineered plants and the method of generating such plants, as presently claimed. In particular, the specification discloses the appropriate elements of the claimed plants together with the appropriate techniques that would effectively produce such plants. Indeed, the specification provides one skilled in the art with the detailed steps deemed necessary to duplicate the claimed method and genetically engineered plants, including methods for generating mutations in other genes encoding enzymes in the Vitamin C biosynthetic pathway, methods for identifying and isolating genes, methods for transforming plants to express genes, and methods for screening and selecting plants having increased levels of Vitamin C. Thus, it is respectfully submitted that the disclosure complies with section 112 fully, in that the description of the various elements of the genetically engineered plants, together with the steps relating to the novel process for making such plants, provides a full, clear and concise instruction to any person reasonably skilled in the art, thus enabling him to make and use the invention without undue experimentation.

In view of the foregoing amendments and remarks, Applicant respectfully submits that these amendments have fully addressed the Examiner's rejections, and that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejection of claims 1-22 and 24-26 as lacking enablement are respectfully requested.

7. Claims 1-22 remain rejected and claims 24-26 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

More particularly, the Examiner maintains that the specification does not describe which enzymes are crucial for vitamin C biosynthesis, their enzymatic activity, or the sequence of any gene encoding any enzyme involved in vitamin C biosynthesis, including that of any gene encoding GMPase, and does not demonstrate the isolation of GMPase genes from plants other

than *Arabidopsis*. Therefore, the Examiner concludes that, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed plants and methods, and given the high level of unpredictability in this art, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

It is respectfully submitted that genes encoding GMPase (including that of *Arabidopsis* and other species), as well as the other enzymes in the Vitamin C pathway, are well known in the art and, as such, are not required to be disclosed in Applicant's specification. However, Applicant's Figure 1 and the specification at page 4, lines 12-16, disclose the enzymes in the Vitamin C pathway. Further, Applicant's specification provides ample guidance for the sequence of the gene encoding GMPase at page 11, lines 5-8, wherein the GenBank accession number is provided. Thus, one of ordinary skill in the art would know that Applicant was in possession of the sequence of the GDP-mannose pyrophosphorylase, as it is well known in the art, and ample guidance thereto also is disclosed in Applicant's specification.

Moreover, it is respectfully submitted that the Examiner's assertion that the unpredictability associated with overexpression of genes in plants has not been overcome is mistaken, in that Applicant's gene encoding GMPase was transformed into plants, thereby generating genetically engineered plants having increased levels of Vitamin C, relative to the progenitor plants. See Applicant's specification at page 13, line 24, through page 17, line 3. Thus, clearly, Applicant's GMPase can be expressed in plants, and clearly such plants have increased levels of Vitamin C, thus overcoming any alleged unpredictability.

In view of the foregoing amendments and remarks, Applicant respectfully submits that these amendments have fully addressed the Examiner's rejections, and that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejection of claims 1-22 and 24-26 as lacking a sufficient written description are respectfully requested.

8. Claims 1-22 and 24-26 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1 and 16 have been amended to overcome this rejection. Specifically, GDP-mannose epimerase has been amended to GDP-D-mannose-3,5-epimerase per the Examiner's suggestion. Regarding GDP-mannose pyrophosphorylase, although it is referred to as GDP-D-mannose pyrophosphorylase in the description of Figure 1, it is also referred to as GDP-mannose pyrophosphorylase throughout the specification. For example, the Examiner is directed to page 17, lines 5-6, which reads "GDP-mannose pyrophosphorylase is an enzyme in the recently proposed plant AsA biosynthetic pathway (Figure 1)". Other instances of GDP-mannose pyrophosphorylase are found on page 3, lines 10-11; page 17, line 7; page 24 (Abstract). Galactonolactone dehydrogenase has been deleted from claims 1 and 16.

Dependent claims 2-15, 17-22 and 24-26, being dependent upon and further limiting independent claims 1 and 16, should be allowable for the same reason, as well as for the additional recitations they contain. Reconsideration and withdrawal of the rejection of claims 1-22 and 24-26 is respectfully requested.

Rejection under 35 U.S.C. § 112, Second Paragraph

9. Claim 20 remains rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The Applicant has amended claim 20 to overcome this rejection. Specifically, as suggested by the Examiner, "comprises" has been replaced with "has". Reconsideration and withdrawal of the rejection of claim 20 is respectfully requested.

Rejection under 35 U.S.C. § 102

10. Claims 1-3, 5-8, 16 and 18-22 remain rejected under 35 U.S.C. § 102(a) as being anticipated by Bauw *et al.* (WO 98/50558).

Independent claims 1 and 16 have been amended to overcome the rejection. More particularly, galactonolactone dehydrogenase has been deleted from these claims. Reconsideration and withdrawal of the rejection of claims 1 and 16 is respectfully requested.

Dependent claims 2-3, 5-8 and 18-22, being dependent upon and further limiting independent claims 1 and 16, should be allowable for the same reason, as well as for the

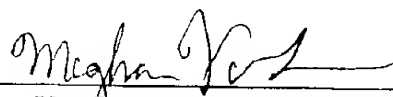
additional recitations they contain. Reconsideration and withdrawal of the anticipation rejection of independent claims 2-3, 5-8, and 18-22 are respectfully requested.

Conclusion

Applicant believes the claims, as amended, are patentable over the prior art, and that this case is now in condition for allowance of all claims therein. Such action is thus respectfully requested. If the Examiner disagrees, or believes for any other reason that direct contact with Applicants' attorney would advance the prosecution of the case to finality, he is invited to telephone the undersigned at the number given below.

"Recognizing that Internet communications are not secured, I hereby authorize the PTO to communicate with me concerning any subject matter of this application by electronic mail. I understand that a copy of these communications will be made of record in the application file."

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4/1/02
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APPENDIX OF AMENDED CLAIMS

1. (Twice Amended) A genetically engineered plant, or portion thereof, comprising a recombinant nucleic acid that encodes an enzyme in a plant Vitamin C biosynthesis pathway, wherein said enzyme is selected from the group consisting of phosphoglucose isomerase, phosphomannomutase, GDP-mannose pyrophosphorylase, and GDP-D-mannose-3,5-[epimerase] and galactonolactone dehydrogenase].
16. (Twice Amended) A method of increasing the level of Vitamin C produced in a plant, or portion thereof, comprising the step of:

engineering said plant, or portion thereof, to express a recombinant nucleic acid that encodes an enzyme in a plant Vitamin C biosynthesis pathway, wherein said enzyme is selected from the group consisting of phosphoglucose isomerase, phosphomannomutase, GDP-mannose pyrophosphorylase, and GDP-D-mannose[3,5-epimerase] and galactonolactone dehydrogenase].
20. (Twice Amended) The method of claim 16 wherein said plant, or portion thereof, has[comprises] increased antioxidation capacity, relative to a progenitor plant from which said genetically engineered plant is derived.